tein from petroleum. Western Hemisphere Nutrition Congress II. San Juan, Puerto Rico. Aug. 26-29, 1968.

(6) Publication 1282. National Academy of Sciences—National Research Council. Washington, D.C. 1966.

(7) Publication 1146. National Academy of Sciences—National Research Council. Washington, D.C. 1964.

(8) Synthetic Organic Chemicals. United States Production and Sales. 1966. Tariff Commission Publication 248. Superintendent of Documents, Government Printing Office, Washington, D.C. 1968.

(9) Schaefer, Arnold E. Epidemiological studies of Vitamin A deficiency. Western Hemisphere Nutrition Congress II. San Juan, Puerto Rico. Aug. 26-29, 1968.

(10) Miller, Sanford A. High energy nonfat nutrient sources. *In* Conference on Nutrition in Space and Related Waste Problems, pp. 343-351. Tampa, Florida. April 27-30, 1964. Publication SP-70. National Aeronautics and Space Administration. Washington, D.C. 1964.

(11) Sonntag, N. O. V. Synthetic fatty acids. *In* E. Scott Pattison, Fatty Acids and Their Industrial Applications. Marcel Dekker, Inc., New York. 1968.

(12) Ehrlich, Paul R. Ballantine Books, Inc. New York. 1968.

(13) Brooke, Clinton L. Fortification of food products with Vitamin A. Western Hemisphere Nutrition Congress II. San Juan, Puerto Rico. Aug. 26-29, 1968.

# Chemical Opposites and Their Ambiguities

**Eduard Farber**

*4530 Brandywine St., N.W., Washington, D. C.*

## Progress through Reversions

In life and in science, the separation of opposites can mean an important step in the right direction, a feat of quick intuition or the result of long investigation. Yet after the opposites have been sharply distinguished and defined, they may be recognized as variously related to each other.

When their relationship is only that of complete opposition involving contradiction, there is the possibility of complete reversion. The Copernican reversion from the geocentric to the heliocentric system is a great historical fact, and it can serve as the model or example for important events in the history of chemistry (1). Other historical examples show us the opposites combined and new unity created out of contradictions. Robert Grosseteste, or Greathead (1175-1253), defined light, which for him was the first form of corporality, as being a spiritual body or a bodily spirit ("corpus spiritualis, sive mavis dicere spiritus corporalis"). Paracelsus (1493-1541), whose great concern was the relationship between human body and spirit, proclaimed triumphantly: "The life of man is nothing else than an astralic balsam, a balsamic ingression, a heavenly and invincible fire." Poetic visions perceive the contradiction between opposites reconciled in a primary unity, which for Grosseteste is light, for Paracelsus life.

The wider the significance of the opposites, the greater the need to combine them in their unity. This rule seems to follow from the nature of opposites. When they are limited and specific, they cannot be so combined, and complete reversion is preferred, or rather specifically justified. Joseph Black performed such a reversion when he demonstrated that instead of the addition of an invisible, fiery principle, it is the loss of a recognizable kind of air that turns mild magnesia into the caustic burnt magnesia, or chalk into quicklime.

Lavoisier reversed the thoughts about the presence of a metallizing agent, which on disappearing also removed the metallic character, and demonstrated the absence of a demetallizing substance which, when added, converted the metal into its "calx."

### The Source of the Ambiguity

Black and Lavoisier were confronted with the specific opposites of positive and negative action, in combination with the general contradiction between presence and absence. Such a combination leads to an ambiguity that can be presented in algebraic symbols. Let the (+) sign stand for presence and for positive action, the (−) sign for absence and for negative action. As in the theory of probability, conjuncture is to be indicated by multiplication. The formulas $(+)\ (+) = (-)\ (-)$ and $(+)\ (-) = (-)\ (+)$ then show that presence combined with positive action is equal to absence combined with negative action, and that the presence of the negative is equal to the absence of the positive. The acceptance (+) of something false (−) produces error (−), and so does the rejection (−) of something true (+).

The simple scheme represents the basis for ambiguities in our theorizing or interpreting, which require and lead to new experiments for a decision. Without using the symbolic signs above, the situation can be described as involving two pairs of either–or opposites at the same time, and the expression "equal to" can be replaced by "looks like." Even with this alternate description, the scheme remains separated from reality by a wide gap; we can bridge the gap by the following discussion, before we fill it with accounts of specific experiences.

For the discussion, we first introduce the observer with the alternates he perceives:

(1) The expected happens: This can mean that an actor is present or that a preventer is absent.

(2) The expected does not happen: The actor is absent or the preventer is present.

(3) The unexpected happens: An unknown actor is present or a known actor is absent.

(4) The unexpected does not happen: We would notice this only if the "unexpected" were actually something at least imagined, which makes this alternative identical with (2) above.

In these formulations, the terms "actor" and "preventer" are wide or indefinite enough to mean a substantial amount of reagent or the small catalytic quantity of a promoter or an inhibitor. The ambiguities are thereby multiplied, as shown in our first specific example.

### The Indophenine Reaction

In his 1882 course of lectures at the University of Zurich, Victor Meyer came to the subject of benzene and was prepared to demonstrate the indophenine reaction. This reaction was quite "modern." Adolf Baeyer had found it in 1879: When a little isatin in sulfuric acid is mixed with a sample of benzene, a beautiful blue color appears. The product looked like indigo. Baeyer coined the name indophenine, with the chemist's usual disregard for philological sensitivities, by adding the first syllable of indigo to a derivative from the Greek work pheinein for "shining" that had previously been introduced into chemistry by Auguste Laurent (1808-1853) and survives in the familiar "phenol." In Meyer's lecture, right before the expectant audience, the experiment failed. The assistant, Traugott Sandmeyer, explained that he had verified the test just before the lecture with a normal sample of benzene from coaltar; for the actual demonstration, however, he had carefully prepared an especially pure benzene from benzoic acid. Meyer immediately promised "to look into this." He saw the following alternatives:

(1) A catalytic impurity is present in the normal benzene from coaltar distillates.

(2) An anticatalytic impurity is present in the "chemical" benzene.

(3) An unknown substance is present in the

coaltar benzene. If so, it would be different from impurities in the other sample.

These deliberations led to the discovery that the "normal" benzene contained thiophen (2). Meyer formed this name by combining the Greek for sulfur with the "phen" from pheinein.

How fortunate that toluene, which really gives the indophenine reaction, was absent from the "chemical" benzene!

Here, an ambiguity according to the second alternative of the general scheme started from the attempt to carry out a chemical reaction. In the following example, the start was the measurement of a physical property, and the further development followed along the third alternative of the scheme.

## The Discovery of Argon

Since 1892, Lord Rayleigh's aim had been to measure the specific gravity of nitrogen with precision. Nitrogen prepared by removing the oxygen (and the carbon dioxide) from air gave values between 2.3100 and 2.3103, whereas nitrogen obtained by decomposing nitric oxide, nitrous oxide, or ammonium nitrate gave 2.2987 to 2.3001. Many tests confirmed that the difference in the second decimal place was beyond the experimental error. Lord Rayleigh thought that the nitrogen prepared from the air was the pure element and the "chemical" nitrogen contained a gas of lower specific gravity. He discussed the findings with William Ramsay, who strongly advocated the assumption that the chemical nitrogen was pure and the atmospheric nitrogen was contaminated by the presence of a heavier gas.

The ambiguities can be formulated as follows:

(1) Heavy nitrogen: Weight-reducer (—) absent (—) = weight-increaser (+) present (+)

(2) Light nitrogen: Weight-reducer (—) present (+) = weight-increaser (+) absent (—).

The assumptions were formally equal but chemically very different. Ramsay's intuition, which was fortified by his knowledge of what Henry Cavendish had found in 1784, proved correct (3).

## Positive and Negative Pressure

An activator is a small quantity of a substance that actuates the transformation of much greater quantities of other substances. When the definition is formulated in this way, the kinship to the primitive concepts of ferment and philosopher's stone is permitted to shine through. An inhibitor is the negative correspondent to an activator. What this relationship between positive and negative means can be generally described in the words of Immanuel Kant: ". . . Negative magnitudes are not negations of magnitudes . . . rather they are, in themselves, truly positive and signify only something that is opposed to the other. Thus, negative attraction is not rest, but rather true repulsion" (4).

In a system that is either activated or inhibited, the main bulk of the substances is presumed to be passive or, at least, dormant, and we remember that Berzelius used this last expression for describing the "catalytic force", as an awakener. Substances do not all need to be awakened; they can be "directly" engaged in activities. Even without activators and inhibitors, however, the logical equivalence between positive and negative can turn into practical ambivalence and become a source of problems. In the history of science, they are at the bottom of discussions on preformation as opposed to new creation (5). Another topic of this discussion is the relationship between positive and negative pressure.

One of its forms occurs in the letter written by Evangelista Torricelli on June 11, 1644 concerning the problem of the vacuum and what was later called the barometer: " . . . It may be supposed that the force that prevents quicksilver from falling, in spite of its nature, has its cause in the interior of the vessel, whether it comes from the vacuum or is caused by some extremely rarefied matter. But I claim that the force is external and that it comes from the outside." The controversy about the existence of a vacuum, in which René Descartes and Blaise Pascal were opponents, is illuminated by a passage in Pierre Guiffard's book of 1647: " . . . There (in Pascal's experiments) is observed that brave nothingness against which so many excellent philosophers have fought for such a long time, that fearful void . . . that fine nothing. . .". While these "excellent philosophers" debated the reality of nothingness, Pascal declared ". . . that Nature has no repugnance to a vacuum; . . . that all the effects that have been attributed to this horror proceed from the gravity and pressure of the air . . " (6).

In 1644, Torricelli rejected a force inside the tube, in which quicksilver was kept from falling, and claimed that an external force was responsible. Formally related to this position is what Michael Faraday wrote in 1834 about "evolved substances" as being expelled from the decomposing mass, in contrast to assuming that they were drawn out by an attraction, from the outside (7). An outside force prevents mercury from following its nature and falling out of the tube. An inside force causes the evolution of substances from a decomposing mass.

According to the view of Walther Nernst, it is also an inside "tension" that causes a substance to dissolve, and a particular form of this tension is responsible for the electrolytic dissolution of a metal (8). In analogy to Faraday's language, dissolving substances expand into the solution; they are not drawn into it by the solvent.

The words of Henri LeChatelier express in greater generality the difference that is here involved. The natural phenomena are of two classes, not with regard to their nature, but according to their directions; they are either spontaneous or provoked. "By its evolution in one sense the system *A* provokes the evolution of a system *B* in the other sense; thereby, *A* loses its property of developing spontaneously, and this is acquired by *B*." This property is the same as the motive power of Carnot, the available energy of Maxwell, the free energy of Helmholtz (9).

Continuing in the direction of LeChatelier's thoughts, Johannes Brönsted (1879-1947) sought the causal relationships in thermodynamics, in preference to the purely mathematical developments (10). The heat absorbed by a system is only the measure of the work in expansion, not its cause. The cause is to be found in the potential. When a gas expands spontaneously, the increase in volume is on the side where initially the pressure was higher; thus, a volume moves from low pressure to high pressure. The intensity factor that belongs together and is conjugate with volume is, therefore, negative pressure. Similarly, surface tension is a negative potential; under its influence the surface increases at the side of the initially higher tension. In these cases, "higher" means greater in negative value (11).

## Positive and Negative Food Factors

The early history of the antineuritic vitamin demonstrates the difficulty in distinguishing between the presence of a negative factor (poison) and the absence of a positive or beneficial factor.

In 1886, the Pekelharing-Winkler Commission studied beri beri (polyneuritis) in the Dutch East Indies. Christiaan Eijkman (1858-1930), as assistant to the Commission, had the good fortune to be there when the disease also broke out among chickens fed with polished rice. It was the time when Louis Pasteur and Robert Koch had dramatically turned the general attention to the importance of microorganisms. The first thoughts had, therefore, been directed to a microbial cause. "Polymorphic bacteria" were actually found in the blood of the victims. The accidental new experience, however, made it seem plausible to connect the cause of beri beri with something in the cortex of native rice. In what manner could this something be responsible? Eijkman assumed it functioned by "neutralizing" a nutritional error. Such error had been established in food containing a relative excess of carbohydrate, an experience summarized by Adalbert Czerny (1863-1941) who designated it as "Mehlnährschaden," i.e., damage through food consisting too exclusively of flour (12). By its symptoms it resembled pellagra.

Gerrit Grijns (1865-1944) described the argument as follows: "One may assume the presence of a nerve-degenerating poison, which is able to originate in the intestinal canal, and of an antidote, which neutralizes the poison or, at any rate, its action. The absence of this antidote would then open the door for the development of polyneuritis and in that case, the development of the disease would depend on the occurrence or non-occurrence of the poison." Grijns was much more in favor of a different argument: "There is also much to be said for the other explanation that we have to do with a partial starvation" (13).

Frederick Gowland Hopkins (1861-1947) described the events in these words: "Eijkman's own earlier teaching as based on his experimental results was that the function of the substance in the cortex was to neutralize a nutritional error due to excess of carbohydrate in a diet of rice. A substance which functions in the neutralization of an error is not the same thing as a substance universally necessary, and it was to the existence of substances of the latter type that my own thoughts had turned. Eijkman did not at first visualise beri beri as a deficiency disease; but the view that the cortical substance in the rice supplied a need rather than neutralized a poison was soon after put forward by Grijns and ultimately accepted by Professor Eijkman" (14).

Hopkins here contributed the new concept of "a substance universally necessary." He thus concluded that the specific deficiency that Grijns had suspected was only an example, and that its cause was the absence of a positive food factor of universal importance. The quantity in which this substance acted was very small; this insight came as a great surprise to the nutritionists, although as biochemists they should have been prepared for it by the development of catalysis. The new experience and explanation did not prove that the idea of a massive "nutritional error" was wrong; its role was stated again when Cicely D. Williams published his investigation of the syndrome for which he used the African (Gold Coast) dialect word *kwashiorkor* (15).

The antineuritic substance, which Hopkins extracted from rice hulls in 1906, soon became an example for the "universally necessary" vitamins. What happened when they were absent was then seen as the result of deficiencies, but it was not entirely unreasonable to explain a dificiency syndrome as being caused by the presence of a poison. New questions arose concerning the ways in which the effects were produced by the vitamins or by the "poisons."

### Promoters of Plant Growth and Their Inhibitors

In 1926, E. Kurasawa reported that an extract from the fungus *Gibberella fujkurai* promoted the growth of certain plants. He did not arouse much interst. The effect was different a few years later when it was discovered that an extract from the coleoptyl of *Avena* plants (oats) contained indoleacetic acid (IAA) which increases the rate of elongation when used in very small quantities at high dilution. As usual in such events, other substances were tried. For a time it seemed that certain diphenols were also growth promoters, or auxins as the class of these special activators was called. These diphenols, especially caffeic acid (3,4-hydroxycinnamic acid) did not long remain in that class. They do not directly promote growth, but only prevent the destruction of IAA by an oxidizing enzyme. New experiments led to the conclusion "that IAA oxidation is usually activated by monophenols and inhibited by diphenols" (16).

A positive action of a promoter was here simulated by the prevention of an inhibitor, according to the formalism (+) =

(—) (—). But this formalism only equates the results without identifying the components that generated these results. In experiments about biological regulations, equation must be sharply distinguished from identification. This is exemplified by the following studies on the effect of previous incubation with "cofactors" on the oxidase of IAA, carried out on peas: "Previous work has shown that a diffusible inhibitor of IAA oxidase is produced in the terminal buds of etiolated peas previously exposed to morphogenically active red light. Preincubation of homogenates of such tissue with manganese ion progressively increases IAA-destroying capacity, while preincubation with 2,4-dichlorophenol decreases this activity. Manganese appeared to activate the enzyme complex by causing a disappearance of inhibitor. The natural inhibitor has been isolated in crystalline form and partially characterized as a flavonol complex" (17).

Parachlorophenoxy-*iso*-butyric acid (PCIB) is an anti-auxin. The inhibition exerted on the growth of *Avena* leaf sections by 100 ppm PCIB was reversed to 55 percent by the addition of 100 ppm IAA. The effect of gibberellic acid on the elongation of the leaf proved to be much more sensitive to the anti-auxin (18).

Under the artificial conditions of our experiments, we encounter the problem of having to differentiate between the presence of a suppressor for an inhibitor and the absence of a promoter for an activator; under natural conditions, inhibitor and activator are often found together. The case of gibberellin (19) is only one among many examples for this kind of regulation in organisms.

The premature application of the rule of Ockham's razor can produce short-circuits in explanations that appear simple and direct yet are chemically wrong. Often, the cause is recognizable as an injudicious combination of positive and negative factors. Thus the phototropism of plants is not a direct and positive response to light. K. Kögl has shown that it occurs because auxin is decomposed by light into lumiauxon. A plant inclines towards the light through the stretching action of the part in the shade, where the auxin content is not diminished relative to that in the light (20).

## Differentiations in the Inhibition of Inhibitors and in the Promotion of Promoters

Presence, absence, inhibitor, and promoter can be used like four universal elements in their various combinations to explain biological reactions. Nevertheless, the right choice of elementary combination is sometimes very difficult to establish and to differentiate from other choices. The following few examples are selected from the lecture by Jacques Monod, given when he received the Nobel Prize on December 11, 1965 (21). His work was mainly concerned with mutants of *Escherichia coli.*

Henri J. Vogel and B. D. Davis experimented with a mutant requiring the addition of arginine or of N-acetylornithine. The enzyme acetylornithinase is formed by the bacteria when they are grown in the presence of the substrate acetylornithine, but not when, instead, arginine is present. The direct conclusion was that the substrate induced the synthesis of its enzyme. Monod pointed out that the facts "could just as well be explained as resulting from an inhibitory effect of arginine as from the inductive effect of acetylornithine." Once the alternative was formulated, it led to new experimental arrangements, and they proved it correct.

In their own research, François Jacob and Jacques Monod tested the synthesis of tryptophan by *E. coli.* "The formation of the sequence of events responsible for the synthesis of trytophan by wild *E. coli* can be repressed by tryptophan. Non-repressible mutants have been isolated, where the repressive effect of tryptophan is abolished for the enzymes of the sequence all at once. Therefore, these mutants have a 'regulation' gene distinct from those genes that determine the capacity to synthesize each individual enzyme. The repressible allele $R^{+}_{try}$ of the regulatory gene is dominant over the non-repressible allele $R^{-}_{try}$ . Its role seems to be to provoke the synthesis, in the presence of tryptophan, of a repressor that inhibits the synthesis of each enzyme belonging to the sequence" (22). Thus, the addition of tryptophan prevents its own synthesis by the bacteria in those mutants, in which tryptophan activates the synthesis of an inhibitor against the enzymes the organism would need for the synthesis of tryptophan.

This experience led Monod to the general conclusion: "Why not suppose . . that induction could be effected by an antirepressor rather than by repression by an anti-inducer?" In the progress of this research, things became so complex that it was necessary to introduce an "operator" system in the organism for explanation.

One last example may show that "simple" explanations are to be mistrusted in biological reactions. This example refers to the stomata of plant leaves. "In the light, high concentrations of $CO_2$ cause stomata to close, and low concentrations cause them to open." The simple explanation would be, that the effect is due to the removal of $CO_2$ by photosynthesis. More intimate study, however, justified the hypothesis that the cause should be sought in "essential products of photosynthesis rather than in the depletion of $CO_2$ near the guard cells." When the concentration of the $CO_2$ is very high, less of this essential product is produced and, therefore, the stomata close (23). The presence of the opening reaction had been thought to follow directly from the absence of $CO_2$; now it seemed more reasonable to suppose that the stomata close when a substance responsible for the opening is absent, or rather, is not present in sufficient amount or concentration.

All these examples point toward the need for introducing quantities as factors to the basic four "universal" components.

## Sources and Solutions of Chemical Ambiguities

Ambiguities are painful and so plentiful that they cannot be avoided; they invite diligent work, which converts them from problem to progress.

This occurs on many fronts. A recent Supreme Court decision in a patent matter starts with the statement: ". . . One may patent only that which is 'useful' " and continues: "As is often the case, however, a simple, everyday word can be pregnant with ambiguity when applied to the facts of life" (24). The same is true for many another "simple word" used for characterizing patentable invention or its opposite, such as novel, equivalent, or obvious. Clear-cut strength is here combined with the insidious weakness of ambiguity (25).

The source of such ambiguity is our effort to conquer reality by dividing it, and to do it in the simplest manner by postulating only two polar opposites. We feel that this is a creative effort, and it provides much satisfaction and profit. In specifying what these opposites are, we follow at first along the lines of old thoughts. Activator and inhibitor, promoter and preventer are not quite as "everyday" words as useful and useless or new and obvious, but they contain much that has become familiar from the old concept of the chemical principles. For them, as for their descendants, the solution of the ambiguity was reached through the experimental test for presence or absence, the isolation of the "principle" as a reproducible substance, and the specification of the effect that characterizes the agent. We started by constructing the opposites as representing our own strong feelings, "in analogy to the notion we have of the soul," to use an expression of Leibniz; then we investigate the relationships they have to each other in their systems of substances and organisms. Instead of absolute opposition, we there find cooperation, and the either-or that seemed so attractive when we discovered it yields to a delicate balance that is much more intriguing for thought and experiment.

(1) E. Farber, Copernicanische Umkehrungen in der Geschichte der Chemie. Osiris *5*, 479-98 (1938).

(2) V. Meyer, Ber. dtsch, chem. Ges. *16*, 1465 (1883).

(3) Lord Rayleigh and William Ramsay. Argon, a new constituent of the atmosphere. Proc. Roy. Soc. *57*, 265-87 (1895).

(4) Immanuel Kant. *Versuch, den Begriff der negativen Grössen in die Weltweischeit einzuführen.* Königsberg, 1763; in the edition by Karl Vorländer, Philosophische Bibliothek, Vol. 46a (Leipzig, 1921), p. 75.

(5) Eduard Farber. Variants of preformation theories in the history of chemistry. Isis *54*, 443-60 (1963).

(6) Rene Dugas. *Mechanics in the 17th century.* Neuchâtel, editions du Griffon, 1958, pp. 206, 211, and 222.

(7) Michael Faraday. XX: Experimental researches in electricity. Eighth Series. Phil. Trans. *124*, 425-70 (1834).

(8) Walther Nernst. *Theoretische Chemie*, Stuttgart, Ferdinand Enke, 1893, pp. 131, 383, 568.

(9) Henri LeChatelier. J. de Physique *23*, 289, 352 (1894).

(10) Prosper Colment. L'énergetique de Henri le Chatelier et celle de J. N. Brønsted. Acta Chemica Scandinavica *3*, 1220-37 (1949).

(11) J. N. Brønsted. The fundamental principles of energetics. Phil. Mag. (7) *29*, 449-70 (1940).

(12) A. Czerny and A. Keller. Des Kimdes Ernährung, Ernährungsstörungen und Ernährungstherapie. Leipzig, Deuticke, 1906.

(13) G. Grijns. Researches on vitamins 1900-1911 and his thesis on the physiology of the nervus opticus. Translated and re-edited by a Committee of Honour on Occasion of his 70th Birthday, Gorinchem, J. Noordyn en Zoon, 1935, pp. 35-7.

(14) F. G. Hopkins. The earlier history of vitamin research. Nobel Prize Lecture (Medicine and Physiology), 1929, p. 61.

(15) Cicely D. Williams. Lancet *229*, vol. 2, 1151-2 (1935). See also J. C. Waterlow, J. Cravioto, and Joan M. Stephen. Protein malnutrition in man. *In* Adv. in Protein Chemistry *15*, 131-238, New York, Academic Press, 1960.

(16) K. V. Thimann, M. Tomaszewski, W. L. Porter, Masaki Furuya, Arthur W. Galston, and Brice B. Stowe. Isolation from peas of cofactors and inhibitors of indole-3-acetic acid oxidase. Nature *193*, 456-7 (1962).

(17) Masaki Furuya and Arthur W. Galston. Effect of in vitro preincubation with cofactors on the activity of indoleacetic acid oxidase in peas, Physiologia Plantarum *14*, 750-66 (1961).

(18) Robert Cleland. The role of endogenous auxin in the elongation of *Avena* leaf sections. Ibid. *17*, 126-35 (1964).

(19) Mary R. Corcoran, Charles A. West, and Bernhard O. Phinney. Natural inhibitors of gibberellin-induced growth. In *Gibberellins*, Adv. in Chem. Series No. 28, 1961. pp. 152-8.

(20) K. Kögl. Chemische, physikalische, und pflanzenphysiologische Untersuchungen über Lumiauxon. Naturwiss. *30*, 392 (1942).

(21) Jacques Monod. From enzymatic adaptation to allosteric transition. Science *154*, 475-83 (1966).

(22) François Jacob and Jacques Monod. Gènes de structure et gènes de régulation dans la biosynthèse des protéines. Compt. rend. *249*, 1282-4 (1959).

(23) Paul E. Waggoner and Israel Zelitch. Transpiration and the stomata of leaves. Science *150*, 1413-20, esp. 1414 (1965).

(24) Official Gazette of the United States Patent Office *833* (Dec. 27, 1966), p. 1349.

(25) Eduard Farber. Patentability and the ambiguities of its principles. The Chemist (New York) *44* (6), 191-6 (1967).